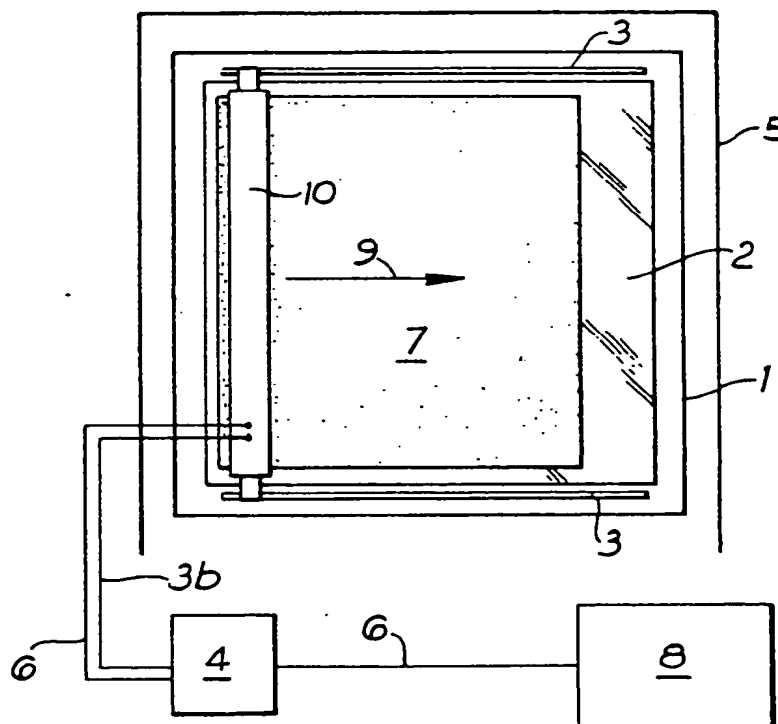


## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(54) Title: SCINTILLATING SHEET SENSOR APPARATUS



## (57) Abstract

The apparatus comprises a CCD mounted in close proximity to a scintillating sheet sample (7) such as a chromatogram or gel, the radiation emitted from the sample being received directly by the CCD. The CCD can be of elongate construction and be scanned across the surface of a sample or can be an  $n \times m$  array, having a very large number of pixels, which is placed directly against the sample sheet.

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SCINTILLATING SHEET SENSOR APPARATUS

This invention relates to an apparatus/assembly for sensing, recording and displaying the patterns of radioactivity in spots, zones or bands that represent the component constituents of chemical or biological samples that have been subject to paper and thin layer chromatography or agarose or polyacrylamide gel electrophoresis and that have been subsequently treated as for conventional fluorography, e.g. by the impregnation of the thin layer with a scintillant.

In the quantitative/qualitative and analytical analysis of chemical and biological compounds, radioactively labelled samples of the compound are frequently separated on the basis of their intrinsic or modified physiochemical properties chromatographically or by molecular sieving in agarose or polyacrylamide matrices. The resulting gel or paper strip or thin-layer plate must then be subjected to a variety of autoradiographic or fluorographic procedures for the detection of the distribution of the underlying radioactivity.

In both direct autoradiography and fluorography the pattern of radioactivity is recorded as an image on a photosensitive emulsion or film.

The disadvantage of this type of procedure is the length of time involved that is required for the image to be recorded, due to the usually low specific radioactivity of the sample components and the limitations of the photographic chemistry.

It is an object of the present invention to provide a device for sensing and recording the patterns of radioactivity in chemical or biological samples that have been subjected to for example paper and thin layer chromatography in a shorter time than with the above described procedure.

According to the present invention there is provided

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apparatus for sensing patterns of radioactivity in prepared biological samples the apparatus comprising means for mounting a sample in a first position and including Charge Coupled Device (CCD) means mounted with  
5 respect to the sample for direct detection of the pattern within the sample.

In a preferred embodiment the present invention provides an assembly comprising a support for the chromatographic strip, thin-layer or gel and a light  
10 detecting sensor consisting of a panel of CCD's, linked to circuits allowing the quantification of light quanta gathered and an analysis of their spatial distribution and storage and visual display and print out of this data both numerically and pictorially. The panel of light  
15 detecting CCD's may consist either of an  $n \times m$  array, sufficiently coextensive with most chromatograms or gels that may be encountered or of a longitudinal fraction of a notional panel of the same dimensions, which is caused to scan laterally and thereby sweep out an equivalent  
20 data gathering area. The assembly may be provided with a light tight enclosure where required, e.g. around the assembly of support, sample object and scanner.

Embodiments of the invention will now be described by way of example with reference to the accompanying  
25 drawings in which:-

Figure 1 diagrammatically shows in plan the essential features of the apparatus with a gel impregnated with scintillant in situ on the supporting  
plate;

30 Figure 2 diagrammatically illustrates the positioning of the dried gel in relation to an  $n \times m$  CCD array in the embodiment of Figure 1; and

Figure 3 diagrammatically illustrates an alternative embodiment utilizing a fibre optic matrix array.

35 Referring to Figure 1 the device comprises a body 1

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in the form of a light tight box containing a supporting plate 2 for the gel 7 or chromatogram which may be secured by means of e.g., suction from beneath or by an overlying optically clear plate or by a suitably configured wire mesh, a frame for the support of the CCD light sensor array configured to hold the array as close as possible to the gel surface while still allowing freedom of movement of the array to scan laterally, in the embodiment illustrated, in conjunction with the electro-mechanical means for effecting the scan in a controlled fashion incorporated into the physical construction of the frame, i.e. guide rails 3 and a motor 3b linked to a servo-mechanism 4 communicating with the control program.

In other embodiments as shown in Figure 2 the frame would allow the direct contact of a more co-extensive  $n \times m$  array 10' (n may be equal to m) by apposition of this array 10' with the gel or chromatogram surface 7. The CCD array 10' may be held in a suitable frame 12 may be lowered down onto the surface of the gel 7.

A light tight enclosure 5, preferably surrounds the CCD and gel to ensure no stray light affects the results. Data lines 6 are provided for communicating the data on light detection from the CCD array to the necessary storage and retrieval and display systems of the control package 8.

Where necessary electronic or electromechanical means are provided for causing the controlled lateral scan of the array in a fashion compatible with the requirements of the data collection package.

It is noted that 7 is sample sheet for illustration only and that arrow 9 represents the direction of initial scan. The scan may be repeated in one or both directions to accumulate data.

With reference now to Figure 3 in an alternative

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embodiment the gel 7 is again placed on a supporting plate 2. The CCD  $n \times n$  detector array 10' is again held in a frame 12 but in addition, a fiber optic matrix 14 is interposed between the array 10' and the gel 7.

5       The  $n \times m$  CCD array may for example comprise 250,000 pixels on an array 5 cms square and the fiber optic matrix 14 may comprise 250,000 short optical fibers suitably grouped together to transmit radiation emitted by the sample stimulated by light 16 from the gel 7 to  
10   the CCD array 10'.

      The array 14 can be fairly deep providing for example a separation of 5, 10 cms or longer between the gel and the CCD array. This may be particularly advantageous if it is required to cool the CCD array to  
15   reduce spurious signals whilst also maintaining the gel  
16   at a higher temperature for ease of handling.

      The fibers 18 within the matrix 14 are preferably of the best available optical transparency such that none of the photons emitted by the gel 7 are  
20   lost.

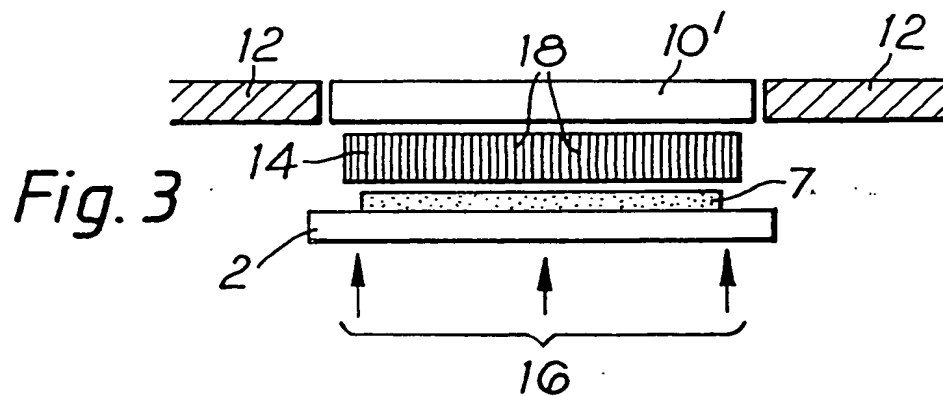
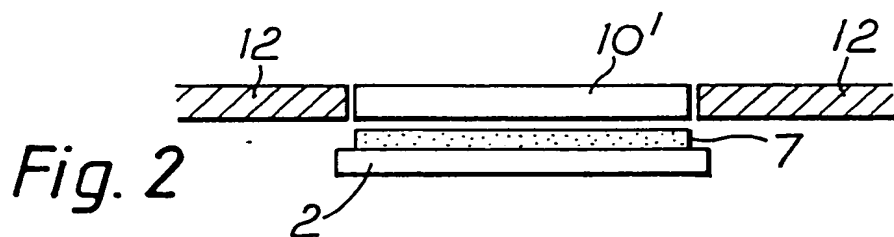
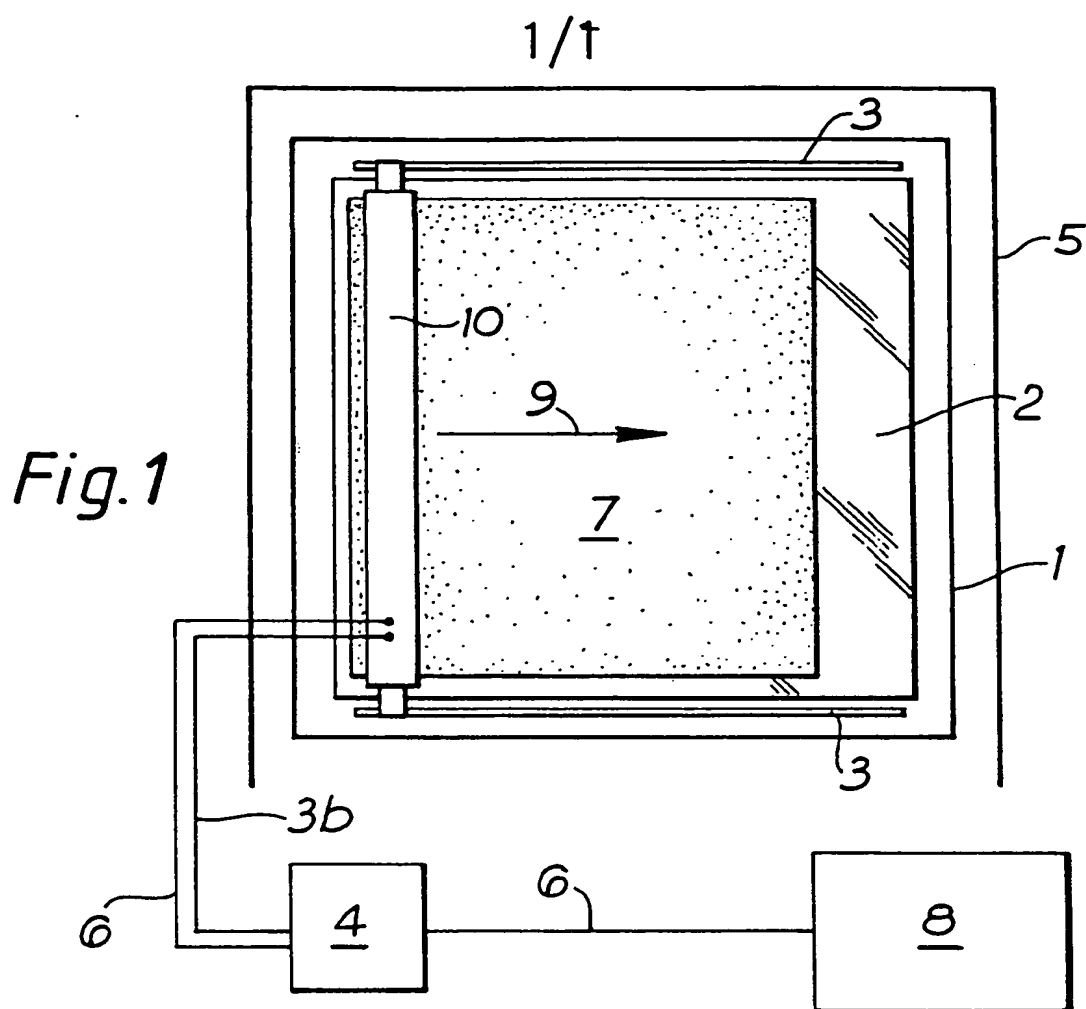
      A fiber optic link can be used in the embodiment of Figure 1, one end of the fiber optic array being scanned across the surface of the sample gel and the other end being placed against the CCD 10 thereby allowing the CCD  
25   10 array to remain static.

      The CCD array may require for example to be cycled every 5 minutes for the more active samples but the time could be 60 minutes or longer for the less active samples. For additional accuracy a number of readings  
30   could be taken, but it may be seen that any particular sample can be analysed in a few hours at the most.

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CLAIMS

1. Apparatus for sensing patterns of radioactivity in prepared biological samples the apparatus comprising means for mounting a sample in a first position and including Charge Coupled Device (CCD) means mounted with respect to the sample for direct detection of the pattern within the sample.
2. Apparatus as claimed in Claim 1 in which the CCD means comprises an elongate detector and includes means for scanning the elongate detector along the sample.
3. Apparatus as claimed in Claim 1 in which the CCD means comprises an  $n \times m$  array which is positioned immediately adjacent to the sample to be in direct contact therewith.
4. Apparatus as claimed in Claim 1 in which the CCD means comprises an  $n \times m$  array and includes a fiber optic matrix comprising a plurality of fibers the fibers being arranged to transmit radiation from the sample to the CCD array, one end of each fiber in the matrix being in contact with the CCD array and the other end being in contact or very close proximity to the sample.
5. Apparatus as claimed in any one of Claims 1 to 4 including means for electronically storing the readout of the CCD means.
6. Apparatus for sensing patterns of radioactivity on prepared biological samples substantially as described with reference to the accompanying drawings.



SUBSTITUTE SHEET



# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 87/00309

<b>I. CLASSIFICATION OF SUBJECT MATTER</b> (if several classification symbols apply, indicate all) * According to International Patent Classification (IPC) or to both National Classification and IPC IPC <sup>4</sup> :        G 01 T 1/00; G 01 T 1/29																				
<b>II. FIELDS SEARCHED</b> <div style="text-align: center; margin-top: 10px;">Minimum Documentation Searched <sup>7</sup></div> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%; padding: 5px;">Classification System</td> <td style="padding: 5px;">Classification Symbols</td> </tr> <tr> <td style="padding: 5px;">IPC<sup>4</sup></td> <td style="padding: 5px;">G 01 T</td> </tr> </table> <p style="text-align: center; margin-top: 10px;">Documentation Searched other than Minimum Documentation to the extent that such Documents are included in the Fields Searched *</p>			Classification System	Classification Symbols	IPC <sup>4</sup>	G 01 T														
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<b>III. DOCUMENTS CONSIDERED TO BE RELEVANT *</b> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 10%; padding: 5px;">Category *</th> <th style="width: 70%; padding: 5px;">Citation of Document, <sup>11</sup> with indication, where appropriate, of the relevant passages <sup>12</sup></th> <th style="width: 20%; padding: 5px;">Relevant to Claim No. <sup>13</sup></th> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">X</td> <td style="padding: 5px;">IEEE Transactions on Nuclear Science, volume NS-32, no. 1, February 1985, IEEE, (New York, US), G.C. Bonazzola et al.: "Charge coupled devices as autoradiography images", pages 567-570 see the whole document</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-3,5,6 4</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">Y</td> <td style="text-align: center; vertical-align: top; padding: 5px;">--</td> <td></td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">Y</td> <td style="padding: 5px;">EP, A, 0143205 (SAUERWEIN) 5 June 1985 see page 1, line 22 - page 2, line 27; page 9, lines 9-19; figures</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-6</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">Y</td> <td style="padding: 5px;">EP, A, 0125691 (FUJI PHOTO FILM CO. LTD) 21 November 1984 see abstract; page 6, line 2 - page 8, line 29; figures</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-6</td> </tr> <tr> <td></td> <td style="text-align: center; padding: 5px;">-----</td> <td></td> </tr> </table>			Category *	Citation of Document, <sup>11</sup> with indication, where appropriate, of the relevant passages <sup>12</sup>	Relevant to Claim No. <sup>13</sup>	X	IEEE Transactions on Nuclear Science, volume NS-32, no. 1, February 1985, IEEE, (New York, US), G.C. Bonazzola et al.: "Charge coupled devices as autoradiography images", pages 567-570 see the whole document	1-3,5,6 4	Y	--		Y	EP, A, 0143205 (SAUERWEIN) 5 June 1985 see page 1, line 22 - page 2, line 27; page 9, lines 9-19; figures	1-6	Y	EP, A, 0125691 (FUJI PHOTO FILM CO. LTD) 21 November 1984 see abstract; page 6, line 2 - page 8, line 29; figures	1-6		-----	
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<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>* Special categories of cited documents: <sup>10</sup></p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"A" document member of the same patent family</p> </div> </div>																				
<b>IV. CERTIFICATION</b> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; padding: 5px;">           Date of the Actual Completion of the International Search  <div style="text-align: center;">10th August 1987</div> </td> <td style="width: 50%; padding: 5px;">           Date of Mailing of this International Search Report  <div style="text-align: center;">31 AUG 1987</div> </td> </tr> <tr> <td style="padding: 5px;">           International Searching Authority  <div style="text-align: center;">EUROPEAN PATENT OFFICE</div> </td> <td style="padding: 5px;">           Signature of Authorized Officer  <div style="display: flex; align-items: center;"> <div style="margin-right: 20px;">ROSSI</div> </div> </td> </tr> </table>			Date of the Actual Completion of the International Search <div style="text-align: center;">10th August 1987</div>	Date of Mailing of this International Search Report <div style="text-align: center;">31 AUG 1987</div>	International Searching Authority <div style="text-align: center;">EUROPEAN PATENT OFFICE</div>	Signature of Authorized Officer <div style="display: flex; align-items: center;"> <div style="margin-right: 20px;">ROSSI</div> </div>														
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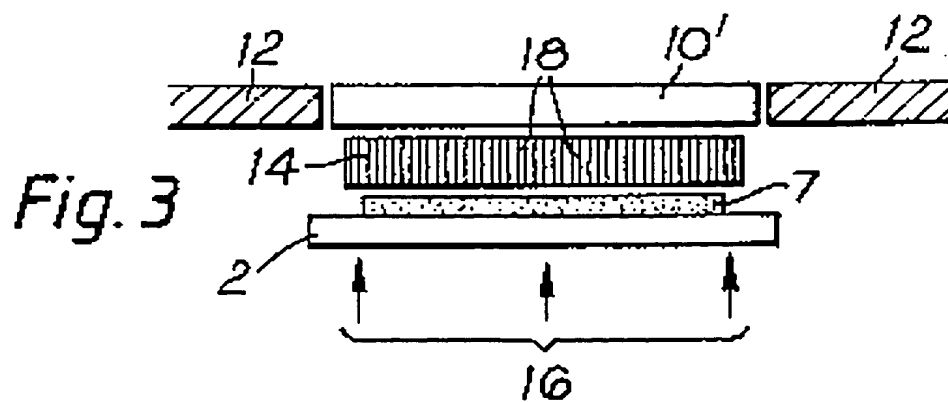
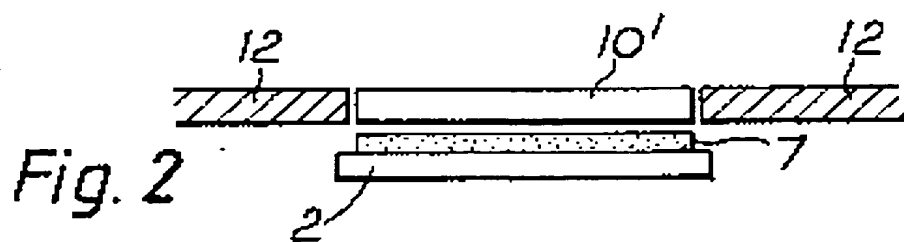
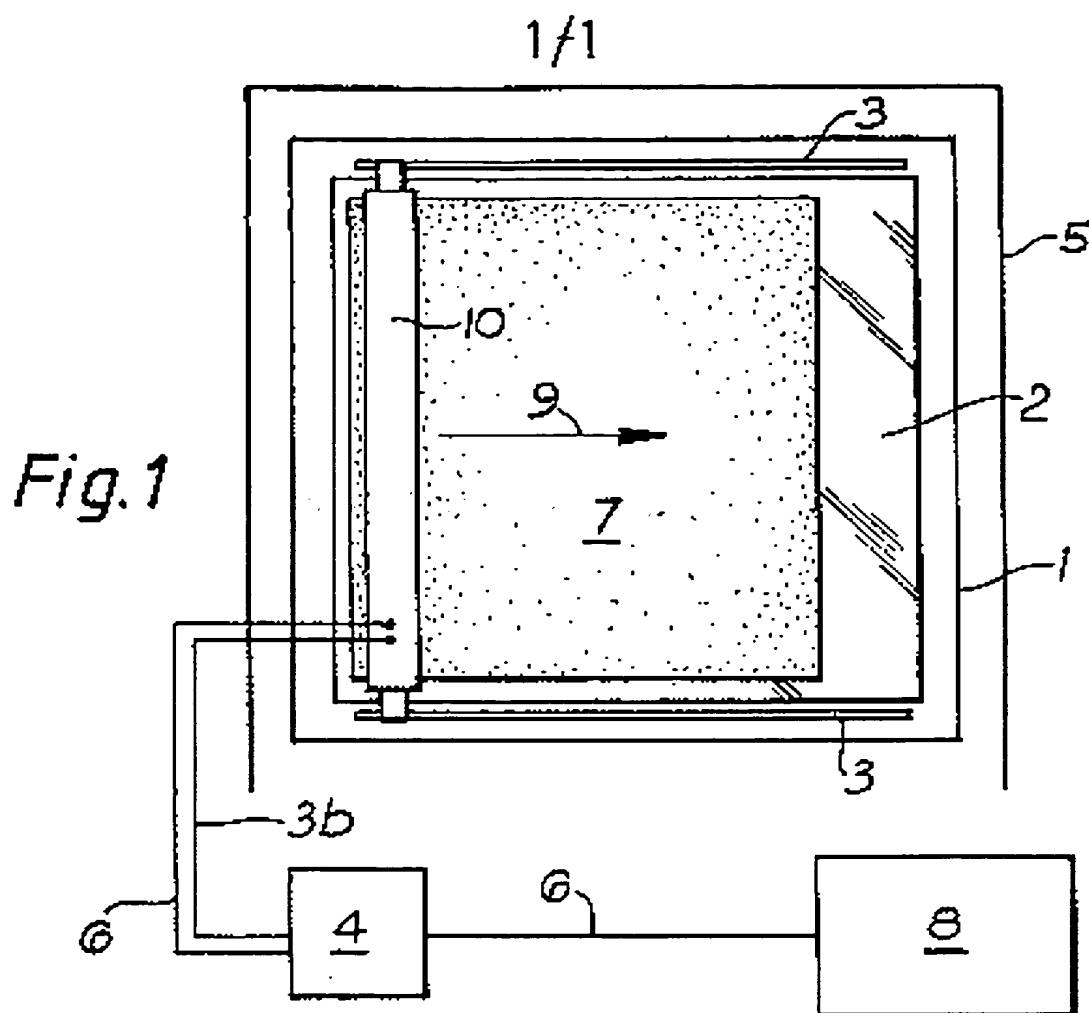
INTERNATIONAL APPLICATION No. PCT/GB 87/00309 (SA 17121)

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A- 0143205	05/06/85	DE-A- 3333738	23/05/85
EP-A- 0125691	21/11/84	JP-A- 59211263	30/11/84
		JP-A- 59211264	30/11/84

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